

AMENDMENTS**In the Specification:**

Page 4, please replace the paragraph starting on line 13, with the following amended paragraph:

Fig. 1 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

Page 4, please replace the paragraph starting on line 18, with the following amended paragraph:

Fig. 2 shows a mass spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3).

Page 4, please replace the paragraph starting on line 21, with the following amended paragraph:

Fig. 3 shows a zoom scan spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3).

Page 4, please replace the paragraph starting on line 24, with the following amended paragraph:

Fig. 4 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH₂ (SEQ ID NO: 4), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

Page 4, please replace the paragraph starting on line 29, with the following amended paragraph:

Fig. 5 shows a mass spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH₂ (SEQ ID NO: 4).

Page 4, please replace the paragraph starting on line 32, with the following amended paragraph:

Fig. 6 shows a zoom scan spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH₂ (SEQ ID NO: 4).

Page 4, please replace the paragraph starting on line 35, with the following amended paragraph:

Fig. 7 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the mixture of the peptide fragments SLSLSP (SEQ ID NO: 3) and SLSLSP-NH₂ (SEQ ID NO: 4), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

Page 5, please replace the paragraph starting on line 8, with the following amended paragraph:

Fig. 10 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion; Fig. 10 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at m/z 660.3 ± 0.5), Fig. 10 C shows that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at m/z 602.3 ± 0.5), and Fig. 10 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at m/z 603.3 ± 0.5).

Page 5, please replace the paragraph starting on line 26, with the following amended paragraph:

Fig. 14 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 1 followed by trypsin digestion; Fig. 14 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at m/z 660.3 ± 0.5), Fig. 14 C shows that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at m/z 602.3 ± 0.5), and Fig. 14 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at m/z 603.3 ± 0.5).

Page 6, please replace the paragraph starting on line 20, with the following amended paragraph:

Fig. 21 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion; Fig. 21 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at $m/z\ 660.3 \pm 0.5$), Fig. 21 C shows that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at $m/z\ 602.3 \pm 0.5$), and Fig. 21 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at $m/z\ 603.3 \pm 0.5$).

Page 20, please replace the paragraph starting on line 26, with the following amended paragraph:

As the materials, the native humanized PM-1 antibody (sometimes referred to as Main), the subtypes 1 and 2 of said antibody, and, as the reference peptides, a peptide Ser-Leu-Ser-Leu-Ser-Pro (SLSLSP) (SEQ ID NO: 3) that is present at the C-terminal of the humanized PM-1 antibody and in which Gly at the C-terminal has been removed and a peptide SLSLSP-NH₂ (SEQ ID NO: 4) in which the C-terminal Pro has been amidated were used. The peptide SLSLSP (SEQ ID NO: 3) and the amidated peptide SLSLSP-NH₂ (SEQ ID NO: 4) were chemically synthesized. The humanized PM-1 antibody Main and the subtypes 1 and 2 of said antibody were obtained by subjecting the humanized PM-1 antibody obtained in Example 1 to a column chromatography and collecting and purifying it by the following method.

Page 22, please replace the paragraph starting on line 13, with the following amended paragraph:

Forty μ l of each sample treated as above was subjected to the liquid chromatography-mass spectrometry (LC-MS/MS). For the reference peptide solutions, i.e. the SLSLSP (SEQ ID NO: 3) solution (SLSLSP (SEQ ID NO: 3) is dissolved in water to make 4 μ M) and the SLSLSP-NH₂ (SEQ ID NO: 4) solution (SLSLSP-NH₂ (SEQ ID NO: 4) is dissolved in water to make 4 μ M), 50 μ l is subjected to the liquid chromatography-mass spectrometry.

Page 22, please replace the paragraph starting on line 33, with the following amended paragraph:

(1) Measurement of the reference peptide fragments

(a) Measurement of the peptide fragment SLSLSP (SEQ ID NO: 3)

Fig. 1 to Fig. 3 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3). The top of Fig. 1 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a chromatogram of a base peak chromatogram. Fig. 2 shows a mass spectrum, and Fig. 3 shows a zoom scan spectrum. The molecular weight (602.2) obtained was in close agreement with the theoretical value (602.3; monoisotopic molecular weight) (Fig. 2 and Fig. 3).

Page 23, please replace the paragraph starting on line 8, with the following amended paragraph:

(b) Measurement of the peptide fragment SLSLSP-NH₂ (SEQ ID NO: 4)

Fig. 4 to Fig. 6 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3). The top of Fig. 4 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a chromatogram of a base peak chromatogram. Fig. 5 shows a mass spectrum, and Fig. 6 shows a zoom scan spectrum. The molecular weight (601.2) obtained was in close agreement with the theoretical value (601.3; monoisotopic molecular weight) (Fig. 5 and Fig. 6).

Page 23, please replace the paragraph starting on line 18, with the following amended paragraph:

(c) Measurement of the mixture of the peptide fragments SLSLSP (SEQ ID NO: 3) and SLSLSP-NH₂ (SEQ ID NO: 4)

Fig. 7 to Fig. 9 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the mixture of the peptide fragment SLSLSP (SEQ ID NO: 3) and SLSLSP-NH₂ (SEQ ID NO: 4). The top of Fig. 7 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a

chromatogram of a base peak chromatogram. Fig. 8 shows the mass spectrum of a peak at a retention time of 44 minutes in Fig. 7, and Fig. 9 shows the mass spectrum of a peak at a retention time of 51 minutes in Fig. 7. The both peptide fragments were completely separated under the condition of the above liquid chromatography.

Page 23, please replace the paragraph starting on line 35, with the following amended paragraph:

Fig. 10 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, the MS chromatogram of SLSLSPG (SEQ ID NO: 5) (selective monitoring at m/z 660.3 \pm 0.5) is shown in Fig. 10 B, that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at m/z 602.3 \pm 0.5) in Fig. 10 C, and that of SLSLSP (SEQ ID NO: 4) (selective monitoring at m/z 603.3 \pm 0.5) in Fig. 10 D. A peak corresponding to SLSLSPG (SEQ ID NO: 5) was detected at 49.7 minutes, but no peptide fragments having the molecular weight of SLSLSP-NH₂ (SEQ ID NO: 4) and SLSLSP (SEQ ID NO: 3) were found.

Page 24, please replace the paragraph starting on line 10, with the following amended paragraph:

Fig. 11 to Fig. 13 show the result of LC-MS/MS analysis of a peptide obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion. The top in Fig. 11 shows a chromatogram detected by a UV at 215 nm and the bottom shows a base peak chromatogram. Fig. 12 shows a mass spectrum of the peak at a retention time of 50 minutes in Fig. 11, and Fig. 13 shows a zoom scan spectrum of the same peak as in Fig. 11. From these results, the detected peak was shown to have the amino acid sequence SLSLSPG (SEQ ID NO: 5). Thus, it was demonstrated that both C-terminals of the H chain of the humanized PM-1 antibody (Main) have the -SLSLSPG (SEQ ID NO: 5) sequence.

Page 24, please replace the paragraph starting on line 25, with the following amended paragraph:

Fig. 14 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 1 followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, Fig. 14 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at m/z 660.3 ± 0.5). Fig. 14 C shows that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at m/z 602.3 ± 0.5), and Fig. 14 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at m/z 603.3 ± 0.5). In addition to a peak corresponding to SLSLSPG (SEQ ID NO: 5) at 47.7 minutes, a peak corresponding to SLSLSP-NH₂ (SEQ ID NO: 4) at 46.2 minutes was noted (though a peak with a molecular weight of 603.3 was noted at about 46 minutes in Fig. 14 D, it is not SLSLSP (SEQ ID NO: 3), based on the retention time).

Page 25, please replace the paragraph starting on line 22, with the following amended paragraph:

From these results, the detected peak was shown to have the amino acid sequences SLSLSPG (SEQ ID NO: 5) and SLSLSP-NH₂ (SEQ ID NO: 4). Thus, it was demonstrated that one of the H chain C-terminals of the humanized PM-1 antibody subtype 1 has the -SLSLSPG sequence (SEQ ID NO: 5), and the other has the -SLSLSPG-NH₂ sequence (SEQ ID NO: 6).

Page 25, please replace the paragraph starting on line 30, with the following amended paragraph:

Fig. 21 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, Fig. 21 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at m/z 660.3 ± 0.5), Fig. 21 C shows that of SLSLSP-NH₂ (SEQ ID NO: 4) (selective monitoring at m/z 602.3 ± 0.5), and Fig. 21 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at m/z 603.3 ± 0.5). Though a peak

corresponding to SLSLSPG (SEQ ID NO: 5) was slightly detected, a peak corresponding to SLSLSP-NH₂ (SEQ ID NO: 4) was more strongly noted (though a peak with a molecular weight of 603.3 was noted at about 45 minutes in Fig. 21 D, it is not SLSLSP (SEQ ID NO: 3), based on the retention time).

Page 26, please replace the paragraph starting on line 7, with the following amended paragraph:

Fig. 22 to Fig. 24 show the result of LC-MS/MS analysis of a peptide obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion. In Fig. 22, the top is a chromatogram detected by a UV at 215 nm and the bottom is a base peak chromatogram. Fig. 23 shows a mass spectrum of the peak at a retention time of 45 minutes in Fig. 22, and Fig. 24 shows a zoom scan spectrum of the same peak as in Fig. 23. From these results, the detected peak was shown to have the amino acid sequence SLSLSP-NH₂ (SEQ ID NO: 4). Thus, it was demonstrated that both of the H chain C-terminals of the humanized PM-1 antibody subtype 2 have the -SLSLSPG-NH₂ sequence (SEQ ID NO: 6).